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EXAMINER
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ART UNIT	PAPER NUMBER
1648	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/856,988	Applicant(s) SCHLOM ET AL.	
	Examiner Bao Qun Li	Art Unit 1648	

-- Th MAILING DATE of this communication appears on th cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-106* is/are pending in the application.

4a) Of the above claim(s) *1-36,38-88 and 94-106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37 and 89-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2 & 19* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence letter* .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV, claims 37 and 89-93 with species of vaccinia vector and dendritic cells as host cells in Paper No. 18 is acknowledged. The traversal is on the ground(s) that examiner has not demonstrated the requisite "serious burden". Applicants' argument has been respectfully considered; however, it is not found persuasive because each group of inventions have different patentable weight and constitute distinct inventions. Therefore, claims 37 and 89-93 with species of vaccinia vector and dendritic cells as host cells are considered before examiner.

2. The requirement is still deemed proper and is therefore made FINAL.

3. Applicants are reminded to amend the claims 37, 89-93 to within the scope of vaccinia virus and dendritic cells for reflecting the examination on the merits.

4. Applicant are also reminded to cancel the claims 1-36, 38-88 and 94-106 drawn to the non-elected groups.

Sequence requirements

This application contains sequence disclosures **on pages 35, 80, 89, 99 and 102** that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required by inserting SEQ ID Nos after each disclosure of sequences on **pages 35, 80, 89, 99 and 102** in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Specification

The following is informality found in the specification:

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 37 and 89-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 37 is indefinite in that the metes and bounds of " a host cell". If Applicants wish to claim to claim a particular cell line that comprises a particular expressing vector, please amend the claim including the precise structural characteristics of the vector. This affects the dependent claims 89-93.

9. Claim 89 is indefinite in that the metes and bounds of "a cell" are not defined. If Applicants wish to claim to claim a particular type of cell, please amend the claim including the precise structural characteristics of the vector. This affects the dependent claims 90-93.

10. Claims 89-91 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the structural relationship of a target antigen or immunological epitope thereof with host cell cited in the claim 89 and the structural relationship of a cytokine, chemokine, flt-3l or recombination thereof with a host cell. This affects the dependent claims 92-93.

Claim Rejections - 35 USC § 101

11. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claim 37 is directed to non-statutory subject matter. Because a host cell can be read on a nature product, especially it can be read on a person's cells that are patentable. It is recommended that claim incorporate the language of "isolated" to overcome the rejection.

Claim Rejections - 35 USC § 112

13. Claims 37 and 89-93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having host dendritic cells (DC) comprising a recombinant poxvirus vector (TRICOM vector) encoding constimulatory molecules of B7-1, ICAM-1 and LFA-3 or the TRICOM vector further comprising a tumor antigen CEA (Fr-CEA/B7-1/ICAM-1/LFA-3, or Fowlpox-cEA-huTRICOM), in which each individual insertions is expressed under separate promoter control, and a method of using the host DC expressing TRICOM vector or Fowlpox-CEA-huTRICOM to activate T lymphocytes in vitro and ex vivo to produce an enhanced antigen specific anti-tumor cytotoxic T-lymphocyte activity for treating a tumor patients, does not reasonably provide enablement for having any or all host cells inserted with any or all three stimulatory molecule in any or all vector to active T cell in vitro and ex vivo for treating or preventing any or all infectious disease and tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

14. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) & 2) State of art and Unpredictability of the filed.

The use host APC cells or tumor cells for expressing a recombinant vector expressing costimulatory molecules B7-1, ICAM-1, LFA-3, optionally further containing an tumor or pathogenic antigen and activating autologous T lymphocyte in vitro and ex vivo treating patients with tumor are know in the art. However, so far there is not approval for curing the cancer patients or preventing any or all infectious disease by the method set forth. This is very unpredictable using the claimed because some of antigen, such as HCV or HIV antigen are not only very week, and no protective neutralizing antigen body has been identified yet.

3) & 4) Number of working examples and Amount of guidance.

Specification only teaches that host DC infected with a recombinant poxvirus vector (TRICOM vector) comprising constimulatory molecules of B7-1, ICAM-1 and LFA-3 or the TRICOM vector further comprising a tumor antigen CEA (Fr-CEA/B7-1/ICAM-1/LFA-3, or Fowlpox-cEA-huTRICOM), in which each individual insertions is expressed under separate promoter control, and a method of using the TRICOM vector or Fowlpox-CEA-huTRICOM to activate Dendritic cells (DC) in vitro and ex vivo active autologous T lymphocyte and produce an enhanced antigen specific anti-tumor cytotoxic T-lymphocyte activity for treating a tumor patients. However, the specification does not teach any or all host cells comprising any or all vector encoding any or all three stimulatory molecules rather than B7-1, ICAM-1 and LFA-3 in any or all vector to active DC in vitro and ex to treat or prevent any or all infectious disease and or tumor. The specification does not teach or give an adequate guidance for which cytokine or chemokine is suitable for the claimed method.

5). Scope of claimed invention.

The breadth and scope of claims read on Gene Therapy or vaccine for treating or preventing any or all tumor or infectious diseases as cited in claims 11, 19-31 and 89-93 and in combination of any or all cytokine or chemokine. Applicants are reminded that these fields are highly unpredictable, whether in gene therapy or vaccine development. Especially considering the general and broad statements in the claims. The in vitro data cannot be extrapolated as a in vivo results.

6) & 7). Nature of the invention and Lever of the skill in the art.

The claimed invention involves one of the most complex and unpredictable field, which requires high technology and an in vivo data to approve that any or all at least three listed

costimulatory molecules, optionally plus an antigen inserted in any or all vector as cited in claim 11 being able to induce an protective immunity for any or all pathogen or tumor as cited in claims 19-31 and 89-93.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 37 and 89-93 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1- 6 of U.S. Patent No. 6,548,068. Although the conflicting claims are not identical, they are not patentably distinct from each other because patent "068" is directed to a host cell infected with a recombinant viral vector comprising multiple costimulatory molecules, such as B7.1, and B7.2, optionally with another immunostimulatory molecule, such as ICAM-3, LFA-3 and a tumor associated antigen, preferably ECA. After about 1-16 hours ex vivo treatment, the activated host T lymphocytes are

administrated to mammal for treatment of cancer. The treatment may be administrated concurrently with other cytokine (lines 3-16 on col. 30). Hence the scope of claimed invention is overlapping with the scope and disclosure of US patent "608".

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

18. Claim 37 is rejected under 35 U.S.C. 102(a) as being anticipated by Zajac et al. (CANCER RESEARCH, October 1998, Vol. 58, pp. 4567-4571).

19. Zajac et al. teach a method for in vitro generation of CTL recognizing tumor-associated antigens (TAAs) by ex vivo treating or infecting an isolated human antigen presenting cells (APC) or primary cultures of skin fibroblasts with a recombinant vaccinia vector encoding costimulatory molecule B7.1 and B7-2 or B7.1/B7.2 plus encoplasmic reticulum-targeted melanoma antigen Mela-A/Mart-1_{27-35}. After cytokine supplementation, an enhanced T cell cytotoxic activity against specific primer antigen peptide has been obtained (See entire document). Therefore, the claimed invention directed to a host cell infected with a recombinant vector comprising multiple costimulatory molecules and a tumor antigen is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 37 and 89-92 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (EP 0733 373A2).

22. Chen et al. disclose a therapeutic composition and a method of using the composition comprising ex vivo treating or transfecting tumor cells, which bears a tumor antigen, with a vector encoding costimulatory molecule B7 and CD2 ligand (LFA-3) and administering the transfected tumor cells to the patients, isolating lymphocytes from the tumor –bearing patients having an immunogenicity effective response to tumor cells, growing the isolated lymphocytes in vitro in the presence of tumor cells or tumor cells transfected to expressing interleukine 2 to increase the number of tumor-reactive cytotoxic T lymphocytes and administering a therapeutic effective dosage of the tumor-reactive cytotoxic T lymphocytes to the tumor bearing patients (See claims 1-22). Therefore, the claimed invention is anticipated by the cited reference.

23. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Oertli et al. (J. Gene. Virol. 1996, Vol. 77, pp. 3121-3125).

24. Oertli et al. disclose a B16.F10 melanoma host cells infected with a recombinant vaccinia vector (pKT1630-B7-1, B7-2) expressing multiple costimulatory moleculeB7-1/B7-2 (See entire document, especially, Fig. 1 on page 3122. Therefore, the claimed invention is anticipated by the cited reference.

25. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Pestka et al. (WO097/00085A1).

26. Pestka et al. disclose a solid tumor vaccine comprising host tumor cells transfected to express interferon-α (INF-α) and an immunomodulatory molecule selected from group consisting of INF-λ, INF-β, IL-2, B7-1, B7-2, ICAM-1 etc. (claims 1-7). Therefore, claimed invention is anticipated by the cited reference.

27. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Parra et al. (Scand. J. Immunol. 1993, Vol. 38, pp. 508-514).

28. Parra et al. disclose a triple transfected CHO cell line co-expressing costimulatory molecules HLA-DR4, B7-1 and LFA-3). Parra et al. teach that the transfected CHO cells used as antigen presenting cells (APCs) in combination of stimulating a cellular antigen by NKI-L16 MoAb activate the naïve and memory CD4+ T cells (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

29. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

30. Claims 37 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldbach-Mansky et al. (Int. Immunol. 1992, Vol. 4, pp. 1315-1360).

31. Goldbach-Mansky et al. disclose several host cell lines expressing LFA-3, ICAM-1 and B7, which include erythroleukemic cell line K562, murine L cells, allo BLCL Raji and human B7 transfected T cells. The CD4+ T cell is activated in the presence of an antigen staphylococcal entertoxin B (SEB) presented by the antigen presenting cells expressing the above metioned costimulatoru molecules (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

32. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

33. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Young et al. (J. Clin. Invest. 1992, Vol. 90, pp. 229-237).

34. Young et al. disclose that isolated human dendritic cells (DC) all express costimulatory molecules B7/BB1 and ICAM-1 and LFA-3. They also test that expression these accessory

molecules expressed on the DC cells activate primary T cells in the allogenic mixed leukocyte reaction (MLR) (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

35. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

36. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Radmayr et al. (Int. J. Cancer 1995, Vol. 63, pp. 627-632).

37. Radmayr et al. disclose a host dendritic cell (DC) line isolated from renal-cell- carcinoma patients in the presence of cytokine G-MCSF or GM-CSF, which express B7-1, B7-2, LFA-3 and ICAM-1 (see entire document, especially, Table I on page 628 and Fig. 2 on page 630). Radmyr et al. also teach that the said dendritic cell line functions as a potent antigen presenting cell (APC) in the PHA-induced proliferation of autologous tumor-infiltrating lymphocytes (TIL) (See lines 19-23 on 2nd col. of page 629 and Table 2 on 631). They concluded that the reproducible growth of blood APC from RCC patients displaying the typical morphologic, phenotypic and functional properties of DC. The availability of autologous dendritic APC allows the design of adoptive therapy protocols involving vaccination with tumor-antigen-loaded DC or in vito generation of tumor-specific T cells, which should be more potent when adoptive returned to the cancer patient than the currently used IL-2 driven TIL (See last paragraph on page 631). Therefore, the claimed invention is anticipated by the cited reference.

38. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227

USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

39. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Hargraves et al. (International Immunology 1995, Vol. 7, pp. 1505-1513).

40. Hargreaves et al. disclose several cell lines isolated from human or mouse, which are transfected with vectors encoding human ICAM-1, human B7.1 and human LFA-3 respectively. (See section of methods on pages 1506 and Fig. 1 on page 1507). Hargreaves et al. also teach that the co-expression of LFA-3 and B7.1 increase the alloproliferative response of adult and cord blood T cells (See lines 14-35 on 1st col. of page 1512). Therefore, the claimed invention is anticipated by the cited reference.

41. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

42. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Vyth-Dreese et al. (Blood 1995, Vol. 85, pp. 2802-2812).

43. Vyth-Dreese et al. disclose 8 lymphoma cell lines isolated from peripheral blood lymphocytes of a patients with follicular B-cell non-hodgkin's lymphoma (B-NHL) immortalized in vitro by Epstein-Barr virus (EBV), termed BNS1, BNS2-1 through BNS2-7. They found that the NS cell lines express LFA-3 and ICAM-1 as well as B7-1 and B7-2 especially cocultured in allo-MLR (Se Table 2 on page 2806, Table 3 & 4 on page 2807). Therefore, the claimed invention is anticipated by the cited reference.

44. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

45. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Wyss-Coray et al. (Eur. J. Immunol. 1993, Vol. 23, pp. 3350-3357).

46. Wyss-Coray et al. disclose several antigen presenting cell lines isolated from human that all express costimulatory molecules LFA_3, ICAM-1 and B7 (Table 2 on 3355). They also teach that use of the isolated antigen presenting cells or some of established antigen presenting cell lines to induce T lymphocyte proliferation and cytokine production in peptide or allospecific T cell clones (See abstract and results on pages 2252-33555). Therefore, the claimed invention is anticipated by the cited reference.

47. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

48. Claims 37 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Delabie et al. (Leuk. Lymphoma 1995, Vol. 18, pp. 35-40).

49. Delabie et al. disclose Reed-Sternberg cells, a neoplastic cells isolated from Hodgkin's disease expressing costimulatory molecules B7, LFA-3 and ICAM-1. In vitro studies have shown

that Hodgkin's disease-derived cell lines potently activate CD4+ T lymphocytes in the mixed lymphocyte activation assay (MLC, mixed lymphocyte culture), suggesting that the Reed-Sternberg cells isolated from Hodgin's disease host function as APC in vivo (See entire document). They teach that Therefore, the claimed invention is anticipated by the cited reference.

50. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in the product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

51. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Cunningham et al. (Journal of Cell Science 1994, Vol. 107, pp. 443-449).

52. Cunningham et al. disclose host alveolar epithelial cells isolated from human lung specimens, wherein the cells express epithelial glycoprotein HEA-125 of MHC class I and class II antigens and other intercellular adhesion molecules ICAM-1, VCAM-1, LFA-3 and B7 (see abstract). Therefore, the claimed invention is anticipated by the cited reference.

53. Applicants are reminded that the claimed invention drawn to a product by process. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts. Therefore, claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 103

54. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

55. Claims 37 and 89-93 are rejected under 35 U.S.C. 103(a) as obvious over Schlom et al. (US Patent No. 6,045,802A) and Radmayr et al. (Int. J. Cancer 1995, Vol. 63, pp. 627-632).

56. Claimed invention drawn to host cell and a method of using a host cells, wherein the host cell is a isolated dendritic cells from patient and is infected with a recombinant vaccinia vector encoding multiple costimulatory molecules, preferably B7.1, B7.2 and LFA-3, optionally further comprising a tumor antigen. The method involves the steps of activating the autologous T lymphocytes by exposing the T lymphocytes with vector-infected DCs and administering the activated T lymphocytes to patients. The method further comprises the administration of a cytokine, chemokine, flt-3 or combination thereof.

57. Schlom et al. disclose a method of using a host cells transfected or infected with a recombinant vaccinia viral vector comprising costimulatory molecule B7-1 and or B7-2 (See lines 7-26 on col. 8) in combination of an tumor antigen, such as ECA for activating host autologous T lymphocyte ex vivo and induce an enhanced cytotoxic activity against specific tumor antigen. Schlom et al. also teach that a cytokine IL-2 can be inserted into same vector that expresses the tumor antigen ECA to enhance the immune response (See lines 56-64 on col. 10). While Schlom et al. does not disclose that the vector can be inserted with other costimulatory factor, such as LFA-3, they suggest that other constimulatory/accessory molecules, e.g. ICAM-1, LFA-3, CD72 rather than B7-1 and B7-2 and cytokines (See lines 25-34 on col. 10) and teach other tumor associated antigen (TAA), viral antigen, such as HIV-gp120, hepatitis B surface antigen, bacterial antigen and yeast antigen can be also used as target antigen incorporated into the vector (lines 29 on col. 9 through line 24 on col. 10). Schlom et al. do not teach to use an

antigen presenting cell DC expressing all three costimulatory molecules: B7, ICAM-1 and LFA-3 to do the autologous activation of T lymphocytes.

58. Radmayr et al. disclose a host dendritic cell (DC) line isolated from renal-cell- carcinoma patients in the presence of cytokine G-MCSF or GM-CSF, which express B7-1, B7-2, LFA-3 and ICAM-1 (See entire document, especially, Table I on page 628 and Fig. 2 on page 630). Radmyr et al. also teach that the said dendritic cell line functions as a potent antigen presenting cell (APC) in the PHA-induced proliferation of autologous tumor-infiltrating lymphocytes (TIL) (See lines 19-23 on 2nd col. of page 629 and Table 2 on 631). They concluded that the reproducible growth of blood APC from RCC patients displaying the typical morphologic, phenotypic and functional properties of DC. The availability of autologous dendritic APC allows the design of adoptive therapy protocols involving vaccination with tumor-antigen-loaded DC or in vitro generation of tumor-specific T cells, which should be more potent when adoptive returned to the cancer patient than the currently used IL-2 driven TIL (See last paragraph on page 631). Therefore, the claimed invention is anticipated by the cited reference.

59. Therefore, it would have been obvious for an ordinary skill in the art to incorporate more costimulatory molecules as suggested by Schlom et al. and shown by Radmayr et al. into a vector that is used for transfecting an antigen presenting cells (APCs) and use the APCs to activate the autologous T lymphocyte as suggested by Radmayr et al. to get more potent activity. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li May 2, 2003

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